

AMENDMENT TO THE CLAIMS

Applicants respectfully request that claims be amended without prejudice, as follows.

Claims 1-9 are hereby cancelled and new claims 10-29 are added. The following listing of claims will replace all prior versions and listings of claims in the application.

IN THE CLAIMS:

1-9. (Cancelled)

10. (New) A method of detecting a modification to a molecule which is labeled with a fluorescent dye by detecting a change in fluorescence lifetime, the method comprising the steps of:

- (a) measuring the fluorescence lifetime of the fluorescently labeled molecule when it is in a first state;
- (b) contacting the molecule with a modifying agent that is capable of changing the molecule from said first state to a second state; and
- (c) measuring the fluorescence lifetime of the fluorescently labeled molecule after contacting with said modifying agent,
wherein a difference in the fluorescence lifetimes measured in (a) and (c) indicates a modification to the molecule.

11. (New) The method of claim 10, wherein the fluorescent dye is coumarine, fluoresceine, rhodamine, oxazine or cyanine.

12. (New) The method of claim 10, wherein the fluorescent dye is covalently or noncovalently coupled to the molecule.

13. (New) The method of claim 10, wherein the fluorescent dye is coupled to the molecule by a spacer.

14. (New) The method of claim 10, wherein the modifying agent is a peptide or

peptidomimetic.

15. (New) The method of claim 10, wherein the modifying agent is an enzyme.

16. (New) The method of claim 15, wherein the enzyme is selected from the group consisting of phosphatases, kinases, phosphodiesterases, and peptidases.

17. (New) The method of claim 10, wherein the modification to the molecule is selected from the group consisting of a change in phosphorylation or dephosphorylation, sulfation or desulfation, methylation or demethylation, oxidization or reduction, acetylation or deacetylation, amidation or deamidation, cyclization or decyclization, a conformational change, a cleavage or addition of an amino acid residue or peptide, coupling of amino acids or peptides to the molecule, ring expansion or ring contraction, aand rearrangement, substitution, elimination, or addition to the molecule.

18. (New) The method of claim 10, wherein molecule in the second state has a difference in a property selected from the group consisting of a state of phosphorylation, sulfation, methylation, oxidization, acetylation, amidation or cyclization of the molecule, respectively, relative to the molecule to the first state.

19. (New) The method of claim 10, wherein the method provides high-throughput screening of a plurality of the molecules or modifying agents.

20. (New) A method of screening for a modifying agent that is capable of modifying a molecule in a first state to a molecule in a second state, wherein the molecule is fluorescently labeled and the fluorescently-labeled molecule in the first state has a different fluorescent lifetime than the fluorescently-labeled molecule in the second state, the method comprising the steps of:

(a) measuring the fluorescence lifetime of the fluorescently-labeled molecule in the first

state;

- (b) contacting the fluorescently-labeled molecule in the first state with a candidate modifying agent;
- (c) measuring the fluorescence lifetime of the fluorescently-labeled molecule after it has been contacted with the candidate modifying agent; and
- (d) comparing the fluorescence lifetimes measured in step (a) and step (c), wherein the candidate modifying agent is identified as a modifying agent where there exists a difference in the fluorescent lifetimes.

21. (New) The method of claim 20, wherein the fluorescent label is coumarine, fluoresceine, rhodamine, oxazine or cyanine.

22. (New) The method of claim 20, wherein the fluorescent label is covalently or noncovalently coupled to the molecule.

23. (New) The method of claim 20, wherein the fluorescent label is coupled to the molecule by a spacer.

24. (New) The method of claim 20, wherein the modifying agent is a peptide or peptidomimetic.

25. (New) The method of claim 20, wherein the modifying agent is an enzyme.

26. (New) The method of claim 25, wherein the enzyme is selected from the group consisting of phosphatases, kinases, phosphodiesterases, and peptidases.

27. (New) The method of claim 20, wherein the modification to the molecule is selected from the group consisting of a change in phosphorylation or dephosphorylation, sulfation or desulfation, methylation or demethylation, oxidization or reduction, acetylation or

deacetylation, amidation or deamidation, cyclization or decyclization, a conformational change, a cleavage or addition of an amino acid residue or peptide, coupling of amino acids or peptides to the molecule, ring expansion or ring contraction, aand rearrangement, substitution, elimination, or addition to the molecule.

28. (New) The method of claim 20, wherein molecule in the second state has a difference in a property selected from the group consisting of a state of phosphorylation, sulfation, methylation, oxidization, acetylation, amidation or cyclization of the molecule, respectively, in relation to the molecule in the first state.

29. (New) The method of claim 20, wherein the method provides high-throughput screening of a plurality of the modifying agents.